What Is the Real Identity of the Mysterious Potential P1, and What Is the Most Important Segment of the Fascicular Ventricular Tachycardia Circuit?

What is the real identity of the mysterious potential P1, and what is the most important segment of the fascicular ventricular tachycardia circuit?

Running Title: Complicated fascicular VT circuit

Akihiko Nogami, MD, PhD

From Cardiovascular Division, University of Tsukuba, Tsukuba, Ibaraki, Japan

Address for correspondence:

Akihiko Nogami, MD, PhD, the Cardiovascular Division, University of Tsukuba, 1-1-1 Tennodai Tsukuba, Ibaraki, 305-8575, Japan.

Tel: +81-29-853-3142 Fax: +81-29-853-3143

E-mail: akihiko-ind@umin.ac.jp

2,270 words

1 figure

20 references

KEY WORDS: catheter ablation, fascicle, Purkinje, ventricular tachycardia

In 1845, Johannes Evangelista Purkinje (Purkyně) discovered gelatinous fibers in the ventricular subendocardium. Later, they were called Purkinje fibers [1]. However, he could not determine the function of that strange tissue and thought it was muscular. In 1906, Sunao Tawara finally described its function as the conducting system (Figure) [2]. In the last three decades, there has been rapid progress in the treatment of ventricular arrhythmias and the Purkinje system has been found to be responsible for the mechanism of some ventricular tachyarrhythmias. These ventricular tachyarrhythmias can be called Purkinje-related arrhythmias, and are manifested as monomorphic ventricular tachycardia (VT) and polymorphic VT, including ventricular fibrillation (VF).

The most common form of idiopathic left ventricular (LV) tachycardia is verapamil-sensitive fascicular tachycardia [3-9]. The underlying mechanism of this tachycardia has been extensively investigated since Zipes et al. first recognized the phenomenon in 1979 [3]. The mechanism of this VT is reentry, because it can be induced, entrained, and terminated by ventricular or atrial stimulation. Many investigators hypothesized that this reentrant VT originates from the Purkinje network near the left posterior fascicle (LPF) [4,7,9,10-13]. Nakagawa et al. first reported the importance of Purkinje potentials in the ablation of this VT [11]. Tsuchiya et al. also reported the significance of a late diastolic potential and emphasized the role of late diastolic and presystolic

potentials in the VT circuit [10]. Ouyang et al. suggested that idiopathic left VT reentry might be a small macroreentry circuit consisting of one anterograde Purkinje fiber with a Purkinje potential, one retrograde Purkinje fiber with retrograde Purkinje potential, and the ventricular myocardium as the bridge [12]. To confirm this reentry circuit, my colleagues and I performed LV septal mapping using a multipolar electrode catheter in patients with LPF-VT [13]. In 15 of 20 patients, 2 distinct sequences of potentials other than LV muscular potential were recorded during VT. We named these potentials P1, a mid-diastolic potential recorded earlier from proximal rather than distal electrodes, and P2, the fused presystolic Purkinje potential recorded earlier from distal electrodes. We demonstrated that P1 represented a critical pathway composed of specialized Purkinje tissue with decremental properties and verapamil-sensitivity. However, strictly speaking, this was not correct. While conduction velocity of P1 is slower than that of other tissues, fascicles, or ventricular myocardium, it is not slow enough to explain this entire VT circuit. If there was no other slower segment in the circuit, its length would be significantly longer and the upper turnaround of the circuit would be outside of the ventricle. The most important segment with decremental properties and verapamil-sensitivity should be present between the ventricular potential and P1, and is not P1 itself; this segment is still missing in intracardiac recordings.

Many investigators demonstrated that P2, which consists of the LPF, is a bystander in the VT circuit [14-16]. Maruyama et al. proved this in an entrainment study in a patient with a large LV false tendon [14]. Morishima et al. also reported a case with negative participation of the proximal LPF in the VT circuit. Although selective capture of the LPF by sinus beats did not affect the VT cycle length, the postpacing interval after entrainment from LV septal myocardium was equal to the cycle length of VT [15]. Maeda et al. directly demonstrated the LPF (P2) to be a bystander during fascicular VT [16]. Immediately after radiofrequency (RF) energy application at a P1-P1 site, the VT (VT1) transitioned to another VT (VT2), and the QRS complexes reflected a more basal exit site with the same tachycardia cycle length. The activation sequence of P2 during VT2 changed, while the activation sequence of the P1 remained unchanged. These findings indicate that P2 is a bystander in VT, but determines the morphology of the VT.

Liu et al. [17] published an excellent article that defines the mechanism of P1 as Purkinje fibers that connect with the LPF at its distal portion and the ventricular myocardium with a slow conduction zone at its proximal region. They demonstrated that the macro-reentrant loop of the LPF-VT involves the ventricular myocardium, a segment of the LPF, a slow conduction zone, and in certain cases, a specially-conducting P1 fiber; the earliest LPF (P2) during LPF-

VT is considered to be the site of connection between P1 and P2, and correlated well with the HV interval during tachycardia. Their schema can explain why P2 is a bystander in the reentry circuit and why the VT cycle length was prolonged with the same QRS morphology after P1-P2 block in their patient no. 8. It can also explain VT in the patient reported by Maeda et al. [16] who had QRS morphological change with the same cycle length after RF energy delivery. The block site in this patient might be just proximal to the P1-P2 junction in P2 (LPF).

We speculated that the origin of this mysterious P1 potential was specialized Purkinje tissue with slow conduction. Conduction velocity of P1 during VT is slower than that of ventricular muscle, fascicles, or Purkinje tissue. However, as Liu et al. speculated, if P1 represents Purkinje fibers that connect with the LPF at its distal segment and the ventricular myocardium with a slow conduction zone at its proximal region, the conduction of P1 during VT is in the reverse direction of that during sinus rhythm. Therefore, slower conduction can be explained by retrograde conduction from the Purkinje-muscle junction to the LPF. Previous investigators and I used a simpler schema as the VT circuit [14-16,18]; however, the real circuit might be more complicated, similar to the Purkinje network in Tawara's monograph (Figure) [2].

Another important finding is that there were two subgroups with

successful ablation sites. We previously found two types of successful ablation sites in verapamil-sensitive LPF-VT. In 15 of 20 patients (75%), RF catheter ablation was successful at the site with a P1 that was distant from the VT exit. After successful ablation, P1 appeared after the QRS complex during sinus rhythm with a sequence identical to that during VT. In the remaining five patients (25%), the P1 could not be detected during VT, but the application of RF current to the VT exit site with a single fused P2 was successful. We speculated that the circuit in the single potential group may involve less of the Purkinje system, or the area of slow conduction may not be close to the endocardial surface [13]. Liu et al. also reported that P1 potentials during VT could not be recorded in every patient. In their study, a P1 potential was recorded in 9 of 14 patients (64%), and VT without a P1 potential was successfully ablated at the earliest P2 sites. We recorded a P1 potential in 75% of patients, and VT without a P1 potential was successfully ablated at the earliest P2 sites. The percentages of subgroups and successful ablation sites in these studies are similar. The speculation is that one of the possible reasons that P1 is not recorded in VT is that the P1 fiber may be short in length and/or non-parallel in orientation with the LPF.

The unresolved missing segment of the circuit is the slow conducting area before P1 that occupies more than half of the cycle length. Liu et al.

hypothesized a unique slow conduction zone between the proximal recorded P1 and the ventricular myocardium. The nature of the slow conduction zone is unknown, but may be ventricular myocardium or an abnormal Purkinje fiber with decremental conduction properties. The histopathologic properties of the P1 fiber and the slow conduction zone involved in the reentry circuit also remain unknown. We examined autopsy specimens from a patient with ischemic cardiomyopathy who underwent RF catheter ablation of VF and VT [19]. In the postmortem examination, fibromuscular bands connecting the posterior papillary muscle and ventricular septum were recognized at the successful ablation sites of the trigger ventricular premature beats, and the microscopic examination revealed Purkinje cells in the center of that fibromuscular band.

Recently, Haïssaguerre et al. classified Purkinje-related monomorphic VT into three subgroups according to the increasing length of the muscular component in their review article [20]: bundle branch reentry VT (shortest muscular component), fascicular-ventricular tachycardia, and Purkinje-muscle reentry (longest muscular component). To decrease circuit size, considerably slower conduction is required to sustain reentry, possibly owing to proportionally more myocardium becoming part of the circuit. However, the cause of slow conduction in the myocardium in a structurally normal heart

remains a mystery. More studies are required to identify the complete mechanism of this complicated tachycardia.

Disclosures

Dr. Akihiko Nogami has received speaker honoraria from St. Jude Medical and an endowment from Medtronic and Johnson & Johnson.

References

1. Purkinje JE. Mikroscopisch-neurologische Beobachtungen. Arch Anat Physiol wiss Med 1845; 12: 281–295.
2. Tawara S. Das Reizleitungssystem des Säugetierherzens - Eine anatomisch - pathlogische Studie über das Atrioventrikularbündel und die Purkinjeschen Fäden. Jena, Verlag von Gustav Fischer, 1906.
3. Zipes DP, Foster PR, Troup PJ, Pedersen DH. Atrial induction of ventricular tachycardia: reentry versus triggered automaticity. Am J Cardiol 1979; 44: 1-8.
4. Belhassen B, Rotmensch HH, Laniado S. Response of recurrent sustained ventricular tachycardia to verapamil. Br Heart J 1981; 46: 679-682.
5. Lin FC, Finley CD, Rahimtoola SH, Wu D. Idiopathic paroxysmal ventricular tachycardia with a QRS pattern of right bundle branch block and left axis deviation: a unique clinical entity with specific properties. Am J Cardiol 1983; 52: 95-100.
6. Klein GJ, Millman PJ, Yee R. Recurrent ventricular tachycardia responsive to verapamil. Pacing Clin Electrophysiol 1984; 7: 938-948.
7. Ohe T, Shimomura K, Aihara N, Kamakura S, Matsuhisa M, Sato I, Nakagawa H, Shimizu A. Idiopathic sustained left ventricular tachycardia: clinical and electrophysiological characteristics. Circulation 1988; 77: 560-568.

8. Okumura K, Matsuyama K, Miyagi H, Tsuchiya T, Yasue H. Entrainment of idiopathic ventricular tachycardia of left ventricular origin with evidence for reentry with an area of slow conduction and effect of verapamil. Am J Cardiol 1988; 62: 727-732.
9. Wen MS, Yeh SJ Wang CC, Lin FC, Wu D. Successful radiofrequency ablation of idiopathic left ventricular tachycardia at a site away from the tachycardia exit. J Am Coll Cardiol 1997; 30: 1024-1031.
10. Tsuchiya T, Okumura K, Honda T, Honda T, Iwasa A, Yasue H, Tabuchi T. Significance of late diastolic potential preceding Purkinje potential in verapamil-sensitive idiopathic left ventricular tachycardia. Circulation 1999; 99: 2408-2413.
11. Nakagawa H, Beckman KJ, McClelland JH, Wang X, Arruda M, Santoro I, Hazlitt HA, Abdalla I, Singh A, Gossinger H, Sweidan R, Hirao K, Widman L, Pitha JV, Lazzara R, Jackman WM. Radiofrequency catheter ablation of idiopathic left ventricular tachycardia guided by a Purkinje potential. Circulation 1993; 88: 2607-2617.
12. Ouyang F, Cappato R, Ernst S, Goya M, Volkmer M, Hebe J, Antz M, Vogtmann T, Schaumann A, Fotuhi P, Hoffmann-Riem M, Kuck KH. Electroanatomic substrate of idiopathic left ventricular tachycardia: Unidirectional block and macroreentry within the Purkinje network.

Circulation 2002; 105: 462-469.

13. Nogami A, Naito S, Tada H, Taniguchi K, Okamoto Y, Nishimura S, Yamauchi Y, Aonuma K, Goya M, Iesaka Y, Hiroe M. Demonstration of diastolic and presystolic Purkinje potential as critical potentials on a macroreentry circuit of verapamil-sensitive idiopathic left ventricular tachycardia. J Am Coll Cardiol 2000; 36: 811-823.
14. Maruyama M, Tadera T, Miyamoto S, Ino T. Demonstration of the reentrant circuit of verapamil-sensitive idiopathic left ventricular tachycardia: direct evidence for macroreentry as the underlying mechanism. J Cardiovasc Electrophysiol 2001; 12: 968-972.
15. Morishima I, Nogami A, Tsuboi H, Sone T. Negative participation of the left posterior fascicle in the reentry circuit of verapamil-sensitive idiopathic left ventricular tachycardia. Heart Rhythm 2012; 23: 556-559.
16. Maeda S, Yokoyama Y, Nogami A, Chik WW, Hirao K. First case of left posterior fascicle in a bystander circuit of idiopathic left ventricular tachycardia. Can J Cardiol. 2014; 30: 1460. e11-13.
17. Liu Q, Shehata M, Jiang R, Yu L, Chen S, Zhu J, Ehdaie A, Sovari AA, Cingolani E, Chugh SS, Jiang C, Wang X. The Macro-reentrant loop in ventricular tachycardia from the left posterior fascicle: New implications for mapping and ablation. Circ Arrhythm Electrophysiol 2016; 9: e004272.

18. Aiba T, Suyama K, Aihara N, Taguchi A, Shimizu W, Kurita T, Kamakura S. The role of Purkinje and pre-Purkinje potentials in the reentrant circuit of verapamil-sensitive idiopathic left ventricular tachycardia. Pacing Clin Electrophysiol 2001; 24: 333–344.
19. Nogami A, Kubota S, Adachi M, Igawa O. Electrophysiologic and histopathologic findings of the ablation sites for ventricular fibrillation in a patient with ischemic cardiomyopathy. J Interv Card Electrophysiol 2009; 24: 133-137.
20. Haïssaguerre M, Vigmond E, Stuyvers B, Hocini M, Bernus O. Ventricular arrhythmias and the His-Purkinje system. Nat Rev Cardiol 2016; 13: 155-166.

Figure Legend

Figure. A macroscopic image of the left ventricle of the human heart. The anterior wall of the left ventricle was cut from just below the aortic valve to the cardiac apex at the line between the anterior and posterior papillary muscles, and opened toward the right and left. Major and small papillary muscles, fibromuscular bands, and connecting tendons are seen (top). The entire course of the left bundle branch and its terminal ramifications are illustrated in red ink on the tracing paper (bottom). Modified from Tawara [2].

Fig 1.